UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,021	09/21/2000	Mary E. Bunkow	240083.508D2	1599

7590 05/20/2002

Gary M Myles PH D
Seed Intellectual Property Law Group PLLC
Suite 6300
701 Fifth Avenue
Seattle, WA 98104-7092

EXAMINER	
JAMROZ, MARGARET E	
ART UNIT	**PAPER NUMBER**
1644	9

DATE MAILED: 05/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,021	BUNKOW ET AL.	
	Examiner	Art Unit	
	Margaret E Jamroz	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment, filed 2/20/2002 (Paper No. 6), is acknowledged.

Claims 94-103 (previously claims 18-19, 22, and 88-93) are pending and are under consideration in the instant application.

2. In view of the amendment filed 2/20/2002 canceling all of the claims and submission of the claims, the previous rejections are hereby withdrawn.

3. The substitute oath or declaration filed on 02/20/2002 (Paper No. 7) is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Inventor David J. Galas did not date the substitute declaration. See 37 CFR 1.52(c).

4. The formal drawings submitted by applicant on 02/20/2002 have been approved by the Draftsman.

The following are new grounds of rejection necessitated by the amendment filed 2/20/2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 98-99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Applicant's amendment, filed 02/20/2002 (Paper No. 6), asserts that no new matter has been added. However, the specification and claims as originally filed do not provide a clear and sufficient support for the limitations "wherein the antibody has an affinity of at least 10^{-7}M" (claim 98) or "wherein the antibody has an affinity of at least 10^{-8}M" (claim 99).

Applicant points to page 44, lines 19-28 for the written description for the above-mentioned "limitations". However, the specification on page 44, lines 19-28 provides written support for antibodies with affinities of "10^{7}M, preferably greater than or equal to 10^{8}M".

The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally-filed. Such limitations introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, Applicant is invited to provide clearly point out the written support for the instant limitations.

6. Claims 94-103 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated antibody (polyclonal, monoclonal, or humanized) or binding fragment thereof which binds to a TGF-beta binding protein encoded by a polynucleotide comprising SEQ ID NOS: 1, 5, 9, 11, 13, and 15, or to TGF-beta binding protein comprising SEQ ID NOS: 2, 6, 10, 12, 14, and 16; an antibody or binding fragment thereof wherein the antibody has an affinity of at least 10^{7}M or 10^{8}M; and a method of producing monoclonal antibodies comprising immunizing an animal with a TGF-beta binding protein comprising SEQ ID NOS: 2, 6, 10, 12, 14, and 16.

Applicant is not in possession of an isolated antibody (polyclonal, monoclonal, or humanized) or binding fragment thereof which binds to an isolated polypeptide encoded by a polynucleotide that specifically hybridizes to a polynucleotide encoding the polypeptides of a polynucleotide sequence comprising SEQ ID NOS: 1, 5, 9, 11, 13, and 15 or complementary sequences thereof (claim 94(c)); an antibody or binding fragment thereof wherein the antibody has an affinity of at least 10^{-7}M or 10^{-8}M; or a method of producing monoclonal antibodies comprising immunizing an animal with any other TGF-beta binding protein.

A description of a protein by functional language in the absence of a structure is not considered sufficient to show possession of the claimed invention. See Fiers, 984 F.2d at 1169-71, 25 USPQ2D at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many species may achieve that result. The definition requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 /f.2d 1516, 1521, 22 USPQ 369, 372-73 (Fed. Cir. 1984) affirming the rejection because the specification does "little more than outline[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of (e.g. structural feature), is not a description of that material.

The instant claims encompass amino acid sequences encoded by nucleic acid molecules that hybridize to nucleic acid sequences not fully complementary to SEQ ID NOS: 1, 5, 9, 11, 13, and 15. The instant specification does not convey to the skilled artisan that the applicant had possession at the time of the invention of an isolated antibody (polyclonal, monoclonal, or humanized) or binding fragment thereof which binds to an isolated polypeptide encoded by a polynucleotide that specifically hybridizes to a polynucleotide encoding the polypeptides of a polynucleotide sequence comprising SEQ ID NOS: 1, 5, 9, 11, 13, and 15 or complementary sequences thereof (claim 94(c)). Further, applicant is not in possession of a method of producing monoclonal antibodies comprising immunizing an animal with any other TGF-beta binding protein.

In view of the aforementioned problems regarding description of the invention claimed, the specification does not provide an adequate written description of the invention claimed herein. Therefore, the skilled artisan cannot envision all the contemplated nucleic acid and amino acid sequence possibilities recited in the instant claims. Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials, conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991). Consequently, a generic statement such as "an isolated polypeptide encoded by a polynucleotide that specifically hybridizes to a polynucleotide encoding the polypeptides of a polynucleotide sequence comprising SEQ ID NOS: 1, 5, 9, 11, 13, and 15 or complementary sequences thereof" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of binding a TGF-beta binding protein and being encoded by a nucleic acid molecule which hybridizes to another nucleic acid molecule that is to some degree complementary to SEQ ID NOS: 1, 5, 9, 11, 13, and 15 or complementary sequences thereof. It does not specifically define any of the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art, therefore, cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function does not suffice to define the genus because it is only an indication of what the property the protein has, an if one extends the analysis in the instant case, what the protein does, rather than what it is. See *In re Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F2d. 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of, is not a description of that material.

Consequently, it is the examiner's position that the requirements of the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 have not been met.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 94-103 are rejected under 35 U.S.C. 102(b) as being unpatentable over U.S. Patent 5,453,492 (AE), of record, as evidenced by Bost et al. (Immunological Investigations, 1988. 17(6&7): 577-586), of record, and Bendayan (The Journal of Histochemistry and Cytochemistry, 1995. 43(9): 881-886), of record, as evidenced by Hay et al. (ATCC Cell Lines and Hybridomas, 8th ed. 1994; pages 149, 258, and 428), and Harlow et al. (Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988, pages 141-157).

The '492 patent teaches antibodies (polyclonal, monoclonal, and humanized) to the TGF-beta binding protein and hybridomas for making the monoclonal antibodies. The '492 patent teaches that the monoclonal antibodies can be made by the methods of Harlow et al. (Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988) which was incorporated by reference (see entire document, but column 6, lines 49-67; and column 7, lines 1-12 in particular).

The cell lines used to generate the TGF-beta binding protein taught in the '492 patent were Hep-G2, Hep-3B, HT-29, and NRK-49F (ATCC cell lines HB 8065, HB 8064, HTB 38, and CRL 1570, respectively; see column 8, lines 40-42 in particular). As is evidenced by Hay et al., the CRL 1570 cell line was obtained from a rat normal kidney fibroblast, and the cell lines HB 8065, HB 8064, HTB 38 were all obtained from human cell lines (see pages 149, 258, and 428 in particular).

SEQ ID NOS: 2 and 6 of the instant application are human sequences and SEQ ID NO: 14 of the instant application is a rat sequence.

Although the '492 patent is silent about the amino acid residues of the TGF-beta binding protein, the recited amino acid sequence is inherently present in the referenced TGF-beta binding protein as they were obtained from the same source. Therefore, even though the '492 patent does not teach specific amino acid sequences of the human and rat TGF-beta binding proteins, they very likely have the same or similar amino acid sequences as the instant SEQ ID NOS: 2, 6, and 14. Further, as is evidenced by Bost et al. and Bendayan, antibodies "cross-react" with antigens with homologous amino acid residues.

As is evidenced by Bost et al., that an antibody "cross-reacts", i.e. binds to more than one protein sequence, does not mean that the antibody does not "specifically bind" with both proteins. Bost et al. (Immunol. Invest. 1988; 17:577-586) describe antibodies which "cross-react" is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). As is evidenced by Bendayan (J. Histochem. Cytochem. 1995; 43: 881-886), only a di-peptide is needed for specific "cross-reactivity" between proteins.

As is evidenced by Harlow et al., a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. a peptide), harvesting spleen cells from said animal, fusing said spleen cells with a myeloma cell line, and culturing said fused cells (i.e. a recombinant host cell capable of producing antibldy) under conditions that allow production of said antibody (see pages 141-157 in particular).

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind to the TGF-beta binding protein recited in the claims.

Therefore, the reference teachings anticipate the claimed invention.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
May 13, 2002

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1600